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L2        38 L1 (3S) (KNOCKOUT OR KNOCK OUT OR TRANSGEN? OR
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L3  ANSWER 1 OF 22  EMBASE  COPYRIGHT 2002 ELSEVIER SCI. B.V.
AN  2002072268 EMBASE
TI  In vivo roles of ROR.alpha. and Sp4 in the regulation of murine prosaposin
    gene.
AU  Jin P.; Sun Y.; Grabowski G.A.
CS  Dr. G.A. Grabowski, Human Genetics Division, Children's Hospital Medical
    Center, 3333 Burnet Ave., Cincinnati, OH 45229-3039, United States.
    greg.grabowski@chmcc.org
SO  DNA and Cell Biology, (2002) 20/12 (781-789).
    Refs: 45
    ISSN: 1044-5498  CODEN: DCEBE8
CY  United States
DT  Journal; Article
FS  022  Human Genetics
    029  Clinical Biochemistry
LA  English
SL  English
AB  Prosaposin has a central role in intracellular glycosphingolipid
    catabolism and also has extracellular functions. This locus is regulated
    temporally and spatially. The highest mRNA expression occurs in the
    central nervous system (CNS) and reproductive system. In vitro, the
    CNS-expressed proteins Sp4 and ***ROR*** .alpha. bind to Sp1 and RORE
    sites within a 310-bp fragment directly upstream of the transcription
    start site. These transcription factors exhibit negative cooperativity in
    vitro for prosaposin expression. Mice deficient in ***ROR*** .alpha.
    and Sp4 (Staggerer [Sg(-/-)] and Sp4 ***knockout*** [Sp4 KO],
    respectively) containing selected prosaposin promoter deletion
    ***transgenes*** were used in comparative expression studies to evaluate
    this negative cooperativity in vivo. Constructs containing the RORE or
    Sp1/U cluster alone were independently stimulatory. Deletion of the Sp1/U
    site led to a decrease in reporter activity only in the cerebellum of
    Sg(-/-) mice. The deletion of RORE and Sp1/U sites did alter the increase
    of reporter activity in the brain and eye, but not in the spinal cord, of
    Sg(-/-) mice. These results indicate that Sp4 and ***ROR*** .alpha.
    play minor and major roles, respectively, in regional expression of the
    prosaposin locus in the brain, whereas expression in the spinal cord is
    independent of ***ROR*** .alpha..

L3  ANSWER 2 OF 22  EMBASE  COPYRIGHT 2002 ELSEVIER SCI.
B.V.DUPLICATE 1
AN  2002177042 EMBASE
TI  Regulation of the TCR.alpha. repertoire by the survival window of
    CD4(+)CD8(+) thymocytes.
AU  Guo J.; Hawwari A.; Li H.; Sun Z.; Mahanta S.K.; Littman D.R.; Krangel
    M.S.; He Y.-W.
CS  Y.-W. He, Department of Immunology, Duke University Medical Center,
    Durham, NC 27710, United States. he000004@mc.duke.edu
SO  Nature Immunology, (2002) 3/5 (469-476).
    Refs: 46
    ISSN: 1529-2908  CODEN: NIAMCZ
CY  United States
DT  Journal; Article
FS  025  Hematology
    026  Immunology, Serology and Transplantation
LA  English
SL  English
AB  T cell receptor (TCR) .alpha. alleles undergo primary and secondary
    rearrangement in double-positive (DP) thymocytes. By analyzing TCR.alpha.
    rearrangement in orphan nuclear receptor ***ROR*** .gamma.-deficient
    mice, in which the DP lifespan is shorter, and in Bcl-x(L)-
    ***transgenic*** mice, in which the DP lifespan is extended, we show
    that the progression of secondary V(.alpha.) to J(.alpha.) rearrangements
    is controlled by DP thymocyte survival. In addition, because Bcl-x(L)
    induces a bias towards 3' J(.alpha.) usage in peripheral T cells, we
    conclude that the programmed cell death of DP thymocytes is not simply a
    consequence of failed positive selection. Rather, it limits the
    progression of rearrangement along the J(.alpha.) locus and the
    opportunities for positive selection, thereby regulating the TCR.alpha.
    repertoire.

L3  ANSWER 3 OF 22  EMBASE  COPYRIGHT 2002 ELSEVIER SCI.
B.V.DUPLICATE 2
AN  2002086604 EMBASE
TI  Age-related phenotypes in the staggerer mouse expand the ROR.alpha.
    nuclear receptor's role beyond the cerebellum.
AU  Jarvis C.I.; Staels B.; Brugg B.; Lemaigre-Dubreuil Y.; Tedgui A.; Mariani
    J.
CS  J. Mariani, Pierre et Marie Curie, CNRS, Neurobiologie Processus
    Adaptatifs, 9 Quai St. Bernard, 75005 Paris, France.
    jean.mariani@snv.jussieu.fr
SO  Molecular and Cellular Endocrinology, (15 Jan 2002) 186/1 (1-5).
    Refs: 39
    ISSN: 0303-7207  CODEN: MCEND6
PUI S 0303-7207(01)00668-2
CY  Ireland
DT  Journal; Article
FS  022  Human Genetics
    008  Neurology and Neurosurgery
LA  English
SL  English
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AB The homozygous mutant mouse staggerer (RORa(sg)/RORa(sg)), was initially described as ataxic, due to the presence of massive neurodegeneration in the cerebellum [Science 136 (1962) 610]. The identification of the widely expressed Retinoic acid receptor-related Orphan Receptor, NR1F1 (***ROR*** .alpha.) gene as the site of mutation in the staggerer mouse has led to great progress in understanding the molecular basis of its phenotype in recent years [Nature 379 (1996) 736]. ***ROR*** .alpha. is a transcription factor, belonging to the nuclear receptor superfamily, for which no natural ligand has yet been identified. Mice engineered for the ***disruption*** of the gene encoding ***ROR*** .alpha. display the same cerebellar atrophic phenotype as the staggerer mouse [Proc. Natl. Acad. Sci. USA 95 (1998) 3960]. More recently, it has been shown that the mutation is semi-dominant, as heterozygous animals display an increased loss of Purkinje cells with age. Furthermore, a number of additional phenotypes outside the nervous system have recently been identified. These include a greater susceptibility to atherosclerosis [Circulation 15 (1998) 2738], immunodeficiencies linked to the overexpression of inflammatory cytokines [J. Neurochem. 58 (1992) 192], abnormalities in the formation and maintenance of bone tissue [Proc. Natl. Acad. Sci. USA 97 (2000) 9197] and changes in muscle differentiation [Nucleic Acids Res. 27 (1999) 411]. Thus, ***ROR*** .alpha. has been directly linked to a number of age-related pathologies of great medical interest. Copyright .COPYRGT. 2002 Elsevier Science Ireland Ltd.

L3 ANSWER 4 OF 22 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.DUPLICATE 3
AN 2001:358248 BIOSIS
DN PREV200100358248
TI Nuclear hormone receptor CHR3 is a critical regulator of all four larval molts of the nematode Caenorhabditis elegans.
AU Kostrouchova, Marta; Krause, Michael; Kostrouch, Zdenek; Rall, Joseph Edward (1)
CS (1) Diabetes Branch, National Institutes of Diabetes Digestive and Kidney Diseases, National Institutes of Health, 9000 Rockville Pike, Building 10, Room 9S213, Bethesda, MD, 20892: JosephR@bdg10.niddk.nih.gov USA
SO Proceedings of the National Academy of Sciences of the United States of America, (June 19, 2001) Vol. 98, No. 13, pp. 7360-7365. print. ISSN: 0027-8424.
DT Article
LA English
SL English
AB CHR3 (nhr-23, NF1F4), the homologue of Drosophila DHR3 and mammalian ***ROR*** /RZR/RevErbA nuclear hormone receptors, is important for proper epidermal development and molting in the nematode Caenorhabditis elegans. ***Disruption*** of CHR3 (nhr-23) function leads to developmental changes, including incomplete molting and a short, fat (dumpy) phenotype. Here, we studied the role of CHR3 during larval development by using expression assays and RNA-mediated interference. We show that the levels of expression of CHR3 (nhr-23) cycle during larval development and reduction of CHR3 function during each intermolt period result in defects at all subsequent molts. Assaying candidate gene expression in populations of animals treated with CHR3 (nhr-23) RNA-mediated interference has identified dpy-7 as a potential gene acting downstream of CHR3. These results define CHR3 as a critical regulator of all C. elegans molts and begin to define the molecular pathway for its function.

L3 ANSWER 5 OF 22 CAPLUS COPYRIGHT 2002 ACS
AN 2002:183277 CAPLUS
DN 137:74339
TI In vivo roles of ROR.alpha. and Sp4 in the regulation of murine prosaposin gene
AU Jin, Peng; Sun, Ying; Grabowski, Gregory A.
CS The Division of Human Genetics, Children's Hospital Research Foundation at Children's Hospital Medical Center, Cincinnati, OH, USA
SO DNA and Cell Biology (2001), 20(12), 781-789
CODEN: DCEBE8; ISSN: 1044-5498
PB Mary Ann Liebert, Inc.
DT Journal
LA English
AB Prosaposin has a central role in intracellular glycosphingolipid catabolism and also has extracellular functions. This locus is regulated temporally and spatially. The highest mRNA expression occurs in the central nervous system (CNS) and reproductive system. In vitro, the CNS-expressed proteins Sp4 and ***ROR*** .alpha. bind to Sp1 and RORE sites within a 310-bp fragment directly upstream of the transcription start site. These transcription factors exhibit neg. cooperativity in vitro for prosaposin expression. Mice deficient in ***ROR*** .alpha. and Sp4 (Staggerer [Sg-/-] and Sp4 ***knockout*** [Sp4 KO], resp.) contg. selected prosaposin promoter deletion ***transgenes*** were used in comparative expression studies to evaluate this neg. cooperativity in vivo. Constructs contg. the RORE or Sp1/U cluster alone were independently stimulatory. Deletion of the Sp1/U site led to a decrease in reporter activity only in the cerebellum of Sg-/- mice. The deletion of RORE and Sp1/U sites did alter the increase of reporter activity in the brain and eye, but not in the spinal cord, of Sg-/- mice. These results indicate that Sp4 and ROR.alpha. play minor and major roles, resp., in regional expression of the prosaposin locus in the brain, whereas expression in the spinal cord is independent of ROR.alpha..
RE.CNT 47 THERE ARE 47 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 6 OF 22 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.DUPLICATE 4
AN 2001278711 EMBASE
TI Cytochrome oxidase activity in the olfactory system of staggerer mutant mice.
AU Deiss V.; Dubois M.; Lalonde R.; Strazielle C.
CS C. Strazielle, Lab. de Microscopie Electronique, Faculte de Medecine, Universite Henri Poincare - Nancy I, allee de la Foret de Haye, Vandoeuvre les Nancy 54500, France. straziel@ciril.fr
SO Brain Research, (10 Aug 2001) 910/1-2 (126-133).
Refs: 49
ISSN: 0006-8993 CODEN: BRREAP
PUI S 0006-8993(01)02678-6
CY Netherlands
DT Journal; Article
FS 008 Neurology and Neurosurgery
011 Otorhinolaryngology
LA English
SL English
AB The staggerer mutation is characterized by the ***disruption*** of a single recessive gene encoding for the nuclear hormone receptor ***ROR*** .alpha.. In addition to the well-studied gene expression in the cerebellum causing massive primary Purkinje cell loss, the ***ROR*** .alpha. gene is also expressed in the thalamus and the olfactory bulb. A quantitative histochemical study of cytochrome oxidase activity was performed in staggerer mutants and their respective controls in order to determine whether olfactory bulb neuropathology leads to neuronal metabolic alterations in olfactory and related limbic regions. In the staggerer olfactory bulb, the core and the shell of the glomeruli had lower levels of cytochrome activity, whereas higher levels were found in the external plexiform and granular layers. Other olfactory and limbic regions were unchanged, except for a higher level in the accessory olfactory bulb and a lower level in the most ventral part of the medial orbital cortex. These results are discussed with regard to the olfactory deficits and changes in social interactions previously observed in this mutant. .COPYRGT. 2001 Elsevier Science B.V. All rights reserved.

L3 ANSWER 7 OF 22 CAPLUS COPYRIGHT 2002 ACS
AN 2000:291059 CAPLUS
DN 132:320946
TI Human retinoid-like orphan receptor gamma
IN Wu, Lin; Chen, Jin-long
PA Tularik Inc., USA
SO PCT Int. Appl., 69 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2000024757	A1	20000504	WO 1999-US24309	19991018

W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRAI US 1998-178358 19981023
AB The invention provides isolated nucleic acid and amino acid sequences of hROR.gamma., antibodies to hROR.gamma., ***transgenic*** animals, methods of identifying ligands for hROR.gamma., and methods of screening for modulators of hROR.gamma.. Members of ***ROR*** .gamma. are preferentially expressed in thymus, T cell lymphomas and skeletal muscle; contain DNA-binding moiety; bind to ligands such as melatonin; and are involved in regulation of immune system (e.g. transcriptional regulation in allergies and inflammatory reactions) and adipocyte differentiation.
RE.CNT 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 8 OF 22 CAPLUS COPYRIGHT 2002 ACS
AN 2000:210338 CAPLUS
DN 132:248254
TI Vectors, cells and transgenic animals for detecting ligands of nuclear receptors
IN Solomin, Ludmila; Mata De Urquiza, Alexander; Perlmann, Thomas
PA Swed.
SO PCT Int. Appl., 55 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2000017334	A2	20000330	WO 1999-IB1682	19990923
WO 2000017334	A3	20000921		

W: AU, JP
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE
AU 9959941 A1 20000410 AU 1999-59941 19990923

EP 1115853 A2 20010718 EP 1999-969436 19990923
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI
PRAI US 1998-101484P P 19980923
WO 1999-IB1682 W 19990923
AB The present invention relates to methods for detection of ligands for nuclear receptors in vivo . In particular, the present invention provides transgenic constructs and transgenic animals, as well as assays using the same to detect ligands for nuclear receptors in transgenic animals. In addn., the invention is useful for analyzing pharmacol. properties of natural and synthetic ligands for nuclear receptors. Thus, transgenic mice were created which expressed (1) chimeric GAL4 (DNA binding domain)-RAR (ligand binding domain) or GAL4-RXR transactivator genes from nestin promoters and (2) GAL4 binding site-controlled lacZ reporter gene. These mice were used in anal. of retinoid ligands during embryogenesis.

L3 ANSWER 9 OF 22 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.DUPLICATE 5
AN 2000317789 EMBASE
TI Retinoid-related orphan receptor .gamma.(ROR.gamma.)is essential for lymphoid organogenesis and controls apoptosis during thymopoiesis.
AU Kurebayashi S.; Ueda E.; Sakaue M.; Patel D.D.; Medvedev A.; Zhang F.; Jetten A.M.
CS A.M. Jetten, Laboratory of Pulmonary Pathology, Natl. Inst. of Envtl. Health Sci., National Institute of Health, Research Triangle Park, NC 27709, United States. jetten@niehs.nih.gov
SO Proceedings of the National Academy of Sciences of the United States of America, (29 Aug 2000) 97/18 (10132-10137).
ISSN: 0027-8424 CODEN: PNASA6
CY United States
DT Journal; Article
FS 029 Clinical Biochemistry
LA English
SL English
AB To identify the physiological functions of the retinoid-related orphan receptor .gamma. (***ROR*** .gamma.), a member of the nuclear receptor superfamily, mice deficient in ***ROR*** .gamma. function were generated by targeted ***disruption*** . ***ROR*** .gamma.(-/-) mice lack peripheral and mesenteric lymph nodes and Peyer's patches, indicating that ***ROR*** .gamma. expression is indispensable for lymph node organogenesis. Although the spleen is enlarged, its architecture is normal. The number of peripheral blood CD3+ and CD4+ lymphocytes is reduced 6- and 10-fold, respectively, whereas the number of circulating B cells is normal. The thymus of ***ROR*** .gamma.(-/-) mice contains 74.4% .+-. 8.9% fewer thymocytes than that of wild-type mice. Flow cytometric analysis showed a decrease in the CD4+CD8+ subpopulation. Terminal deoxynucleotidyltransferase-mediated dUTP nick end labeling (TUNEL) staining demonstrated a 4-fold increase in apoptotic cells in the cortex of the thymus of ***ROR*** .gamma.(-/-) mice. The latter was supported by the observed increase in annexin V-positive cells. ***ROR*** .gamma.(-/-) thymocytes placed in culture exhibit a dramatic increase in the rate of 'spontaneous' apoptosis. This increase is largely associated with CD4+CD8+ thymocytes and may, at least in part, be related to the greatly reduced level of expression of the anti-apoptotic gene Bcl-X(L). Flow cytometric analysis demonstrated a 6-fold rise in the percentage of cells in the S phase of the cell cycle among thymocytes from ***ROR*** .gamma.(-/-) mice. Our observations indicate that ***ROR*** .gamma., is essential for lymphoid organogenesis and plays an important regulatory role in thymopoiesis. Our findings support a model in which ***ROR*** .gamma. negatively controls apoptosis in thymocytes.

L3 ANSWER 10 OF 22 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.DUPLICATE 6
AN 2000211217 EMBASE
TI Down-regulation of the orphan nuclear receptor ROR.gamma.t is essential for T lymphocyte maturation.
AU He Y.-W.; Beers C.; Deftos M.L.; Ojala E.W.; Forbush K.A.; Bevan M.J.
CS Dr. M.J. Bevan, Howard Hughes Medical Institute, Department of Immunology, Univ. of Washington Sch. of Medicine, Seattle, WA 98195, United States. mbevan@u.washington.edu
SO Journal of Immunology, (2000) 164/11 (5668-5674).
Refs: 32
ISSN: 0022-1767 CODEN: JOIMA3
CY United States
DT Journal; Article
FS 026 Immunology, Serology and Transplantation
LA English
SL English
AB Thymocyte development is a tightly regulated process. CD4+ CD8+ double-positive (DP) immature thymocytes exhibit distinct phenotypic features from mature T cells; they express only 10% of surface TCR that are found on mature T cells and do not proliferate and produce IL-2 in response to stimulation. In this report we show that ***transgenic*** expression of the orphan nuclear receptor ***ROR*** .gamma.t in mature T cells down-regulates their surface TCR expression. The ***ROR*** .gamma.t ***transgene*** inhibits IL-2 production by mature T cells, and this inhibition may be partially due to the inhibitory effect of ***ROR*** .gamma.t on c-Rel transcription. Furthermore, ectopic expression of ***ROR*** .gamma.t inhibits the proliferation of mature and immature T cells. These results, together with its predominant expression in DP thymocytes, suggest that ***ROR*** .gamma.t controls these distinct phenotypic features of DP thymocytes. Our data suggest that down-regulation of ***ROR*** .gamma.t expression in thymocytes is essential for their maturation.

L3 ANSWER 11 OF 22 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.DUPLICATE 7
AN 2001008259 EMBASE
TI Prosaposin: Promoter analysis and central-nervous-system-preferential elements for expression in vivo.
AU Sun Y.; Jin P.; Witte D.P.; Grabowski G.A.
CS G.A. Grabowski, Div. and Program in Human Genetics, Children's Hospital Medical Center, TCHRF 1042, 3333 Burnet Avenue, Cincinnati, OH 45229-3039,
United States. grabg0@chmcc.org
SO Biochemical Journal, (1 Dec 2000) 352/2 (549-556).
Refs: 32
ISSN: 0264-6021 CODEN: BIJOAK
CY United Kingdom
DT Journal; Article
FS 029 Clinical Biochemistry
LA English
SL English
AB The expression of prosaposin is temporally and spatially regulated at the transcriptional and post-translational levels. In vitro, the mouse prosaposin promoter contains functional RORE [retinoic acid-receptor-related orphan receptor .alpha. subunit (***ROR*** .alpha.)-binding element], Sp1 and U (unknown) sites within 310 bp directly 5' to the transcription start site and additional elements within 2400 bp 5' to the transcription start site. To elucidate promoter regions important to tissue-preferential expression in vivo, ***transgenic*** mice were created with 5'-flanking deletions of the prosaposin gene fused to a luciferase reporter. Nearly exclusive expression was observed in cerebrum, cerebellum and eyes of adult ***transgenic*** mice containing constructs with 234-310 bp of 5'-flanking DNA. This central nervous system (CNS) expression was due to the presence of RaRE and overlapping Sp1 sites in this region. Internal deletion of RORE and the Sp1 cluster from the longer constructs with 2400 bp of 5'-flanking DNA significantly diminished expression in the CNS. The appearance of substantial visceral tissue (e.g. liver, spleen, lung, kidney, thymus and heart) expression was obtained with ***transgenic*** mice bearing constructs with 742-2400 bp of 5'-flanking DNA. The cellular localization of luciferase reportergene expression from these constructs corresponded closely with that for prosaposin. These results define important CNS and visceral regulatory regions in the promoter in viva and may be sufficient to account for the majority of prosaposin's tissuepreferential expression.

L3 ANSWER 12 OF 22 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.DUPLICATE 8
AN 1999:175895 BIOSIS
DN PREV199900175895
TI RORalpha augments thyroid hormone receptor-mediated transcriptional activation.
AU Koibuchi, Noriyuki (1); Liu, Ying; Fukuda, Harumi; Takeshita, Akira; Yen, Paul M.; Chin, William W.
CS (1) Division of Genetics, Department of Medicine, Brigham and Women's Hospital, 75 Francis Street, Thorn 1004, Boston, MA, 02115 USA
SO Endocrinology, (March, 1999) Vol. 140, No. 3, pp. 1356-1364.
ISSN: 0013-7227.
DT Article
LA English
AB This study is designed to clarify the role of an orphan nuclear hormone receptor, RORalpha, on thyroid hormone (TH) receptor (TR)-mediated transcription on a TH-response element (TRE). A transient transfection study using various TREs (i.e., F2 (chick lysozyme TRE), DR4 (direct repeat), and palindrome TRE) and TR and RORalpha1 was performed. When RORalpha1 and TR were cotransfected into CV1 cells, RORalpha1 enhanced the transactivation by liganded-TR on all TREs tested without an effect on basal repression by unliganded TR. By electrophoretic mobility shift assay, on the other hand, although RORalpha bound to all TREs tested as a monomer, no (or weak) TR and RORalpha1 heterodimer formation was observed on various TREs except when a putative ***ROR*** -response element was present. The transactivation by RORalpha1 on a ***ROR*** -response element, which does not contain a TRE, was not enhanced by TR. The effect of RORalpha1 on the TREs is unique, because, whereas other nuclear hormone receptors (such as vitamin D receptor) may competitively bind to TRE to exert dominant negative function, RORalpha1 augmented TR action. These results indicate that RORalpha1 may modify the effect of liganded TR on TH-responsive genes. Because TR and RORalpha are coexpressed in cerebellar Purkinje cells, and perinatal hypothyroid animals and RORalpha-***disrupted*** animals show similar abnormalities of this cell type, cross-talk between these two receptors may play a critical role in Purkinje cell differentiation.

L3 ANSWER 13 OF 22 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
AN 1999:438246 BIOSIS
DN PREV199900438246
TI ***Ror*** -2 ***knockout*** mice exhibit deformed cartilage anlagen and retarded growth of long bones.
AU Kimble, R. B. (1); Wu, D. (1); Liu, X. (1); Poueymirou, W. T. (1); DeChiara, T. M. (1); Stahl, N. (1); Yancopoulous, G. D. (1)

CS (1) Regeneron Pharmaceuticals, Tarrytown, NY USA
SO Journal of Bone and Mineral Research, (Sept., 1999) Vol. 14, No. SUPPL. 1, pp. S156.
Meeting Info.: Twenty-First Annual Meeting of the American Society for Bone and Mineral Research St. Louis, Missouri, USA September 30-October 4, 1999 American Society for Bone and Mineral Research
. ISSN: 0884-0431.
DT Conference
LA English

L3 ANSWER 14 OF 22 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
AN 1999084699 EMBASE
TI Mechanisms underlying neurological abnormalities resulting from developmental hypothyroidism.
AU Koibuchi N.; Chin W.W.
CS Dr. N. Koibuchi, Division of Genetics, Department of Medicine, Brigham and Women's Hospital, 75 Francis Street, Boston, MA 02115, United States
SO Current Opinion in Endocrinology and Diabetes, (1999) 6/1 (26-32).
Refs: 63
ISSN: 1068-3097 CODEN: CENDES
CY United States
DT Journal; General Review
FS 003 Endocrinology
005 General Pathology and Pathological Anatomy
008 Neurology and Neurosurgery
021 Developmental Biology and Teratology
LA English
SL English
AB Perinatal hypothyroidism may result in abnormal development of the central nervous system, or cretinism in man. However, the molecular mechanisms of thyroid hormone (TH) action involved in this process are not yet fully understood. To study such mechanisms, the developing rodent cerebellum during the perinatal period can be an excellent model system. Recently, a mutant mouse, staggerer (sg), which exhibits morphological and neurological abnormalities of the cerebellum similar to those seen in hypothyroid animals, has been shown to result from the homozygous ***disruption*** of the orphan nuclear hormone receptor, ***ROR*** .alpha. gene. In this mouse, TH does not alter the abnormal phenotype nor normalize pcp-2 gene (TH-regulated) expression, although tissue TH receptor (TR) and serum TH levels are normal. We have recently confirmed the involvement of ***ROR*** .alpha. in TH-mediated regulation of neuronal differentiation. In addition, it has been shown that TH action on cerebellar development may be mediated at least in part by brain-derived neurotrophic factor (BDNF) and neurotrophin-3 (NT-3), members of the neurotrophic factor family that serve critical roles in neurite growth and synaptogenesis. These findings may provide new insights in the molecular mechanisms of TH action in neuronal development and differentiation.

L3 ANSWER 15 OF 22 CAPLUS COPYRIGHT 2002 ACS
AN 1998:518349 CAPLUS
DN 129:228787
TI Disruption of retinoid-related orphan receptor .beta. changes circadian behavior, causes retinal degeneration and leads to vacillans phenotype in mice
AU Andre, Elisabeth; Conquet, Francois; Steinmyr, Markus; Stratton, Sharon C.; Porciatti, Vittorio; Becker-Andre, Michael
CS Geneva Biomedical Research Institute, Glaxo Wellcome Research and Development S.A., Plan-les-Ouates, CH-1228, Switz.
SO EMBO Journal (1998), 17(14), 3867-3877
CODEN: EMJODG; ISSN: 0261-4189
PB Oxford University Press
DT Journal
LA English
AB The orphan nuclear receptor ROR.beta. is expressed in areas of the central nervous system which are involved in the processing of sensory information, including spinal cord, thalamus and sensory cerebellar cortices. Addnl., ROR.beta. localizes to the three principal anatomical components of the mammalian timing system, the suprachiasmatic nuclei, the retina and the pineal gland. ROR.beta. mRNA levels oscillate in retina and pineal gland with a circadian rhythm that persists in const. darkness. ROR.beta.-/- mice display a duck-like gait, transient male incapability to sexually reproduce, and a severely disorganized retina that suffers from postnatal degeneration. Consequently, adult ROR.beta.-/- mice are blind, yet their circadian activity rhythm is still entrained by light-dark cycles. Interestingly, under conditions of const. darkness, ROR.beta.-/- mice display an extended period of free-running rhythmicity. The overall behavioral phenotype of ROR.beta.-/- mice, together with the chromosomal localization of the ROR.beta. gene, suggests a close relationship to the spontaneous mouse mutation vacillans described >40 yr ago.

L3 ANSWER 16 OF 22 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.DUPLICATE 9
AN 1998380797 EMBASE
TI ROR.alpha. gene expression in the perinatal rat cerebellum: Ontogeny and thyroid hormone regulation.
AU Koibuchi N.; Chin W.W.
CS Dr. N. Koibuchi, Division of Genetics, Department of Medicine, Brigham and Women's Hospital, 75 Francis Street, Boston, MA 02115, United States.
koibuchi@rascal.med.harvard.edu
SO Endocrinology, (1998) 139/5 (2335-2341).
Refs: 32
ISSN: 0013-7227 CODEN: ENDOAO
CY United States
DT Journal; Article
FS 003 Endocrinology
021 Developmental Biology and Teratology
037 Drug Literature Index
LA English
SL English
AB Deficiency of thyroid hormone (TH) during the perinatal period results in severe neurological abnormalities in rodent cerebellar development. However, the molecular mechanisms of TH action in the developing cerebellum are not fully understood. Of note, a mutant mouse, staggerer, in which the orphan nuclear hormone receptor ***ROR*** .alpha. gene is ***disrupted*** , exhibits cerebellar abnormalities similar to those seen in the hypothyroid animals, despite normal thyroid function. We, therefore, speculated that TH (tetraiodo-L- thyronine; T4) may regulate ***ROR*** .alpha. gene expression, which then may regulate genes essential for normal brain development. To test this hypothesis, we studied the changes in ***ROR*** .alpha. gene expression in perinatal hypothyroid rat cerebellum and the effect of TH replacement using Northern blot analysis, ribonuclease protection assay and in situ hybridization histochemistry. During cerebellar development, an approximately 3-fold increase in the cerebellar content of ***ROR*** .alpha. messenger RNA (mRNA) was seen in both propylthiouracil-treated, and propylthiouracil-treated and T4-replaced animals. However, the increase was accelerated when T4 was injected, although the ***ROR*** .alpha. mRNA content was identical, with or without T4, by 30 days alter birth (P30). In contrast, T4 treatment suppressed the TH receptor .alpha.1 and c-erbA.alpha.2 mRNA content by P30; retinoic acid X receptor-.beta. mRNA content was not influenced by thyroid status. A significant hybridization signal for ***ROR*** .alpha. mRNA was seen only over Purkinje cells in the cerebellar cortex by in situ hybridization histochemistry. These results indicate that TH alters the timing of expression of the ***ROR*** .alpha. gene in the Purkinje cells of the cerebellar cortex, which may, in turn, influence Purkinje cell differentiation.

L3 ANSWER 17 OF 22 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.DUPLICATE 10
AN 1998083271 EMBASE
TI Orphan nuclear receptor ROR.alpha.-deficient mice display the cerebellar defects of staggerer.
AU Dussault I.; Fawcett D.; Matthyssen A.; Bader J.-A.; Giguere V.
CS V. Giguere, Molecular Oncology Group, Royal Victoria Hospital, 687 Pine Avenue West, Montreal, Que. H3A 1A1, Canada.
vgiguere@dir.molonc.mcgill.ca
SO Mechanisms of Development, (1998) 70/1-2 (147-153).
Refs: 35
ISSN: 0925-4773 CODEN: MEDVE6
PUI S 0925-4773(97)00187-1
CY Ireland
DT Journal; Article
FS 021 Developmental Biology and Teratology
LA English
SL English
AB It has recently been shown that the neurological mutant mouse staggerer (sg) harbors a deletion within the Rora gene that encodes the orphan nuclear receptor ***ROR*** .alpha.. This deletion removes an exon encoding part of the ligand binding domain of the putative receptor, generating an ***ROR*** .alpha. truncated protein (***ROR*** .alpha.(sg)). It is unknown whether sg acts as a null or highly hypomorphic allele. To address this question, we have generated a null mutation of Rora by targeted ***disruption*** of its DNA binding domain in ES cells. The ***Ror*** .alpha.+ mice are viable but display tremor, body imbalance, small size and die between 3-4 weeks, similar to the sg mouse. Histological examination of the cerebellum of ***Ror*** .alpha.+ and sg mice showed similar defects, including small size and fewer ectopically localized Purkinje cells. Northern blot analysis of cerebellar RNA showed that ***ROR*** .alpha. transcripts are still expressed in the ***Ror*** .alpha.+ and sg mutants, although with altered mobilities. However, the cerebellum of the ***Ror*** .alpha.+ mutant does not express the ***ROR*** .alpha. protein. Attempts to complement the defect of the ***Ror*** .alpha.+ with sg failed, demonstrating conclusively that the sg defects are caused by the absence of functional ***ROR*** .alpha..

L3 ANSWER 18 OF 22 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.DUPLICATE 11
AN 1998268215 EMBASE
TI The potential role of the transcription factor RZR/ROR as a mediator of nuclear melatonin signaling.
AU Wiesenberg I.; Missbach M.; Carlberg C.
CS Dr. C. Carlberg, Institut fur Physiologische Chemie I, Heinrich-Heine-Univ. Dusseldoff, Postfach 10 10 07, D-40001 Dusseldorf, Germany. carlberg@uni-duesseldorf.de
SO Restorative Neurology and Neuroscience, (1998) 12/2-3 (143-150).
Refs: 54
ISSN: 0922-6028 CODEN: RNNEEL
CY Ireland
DT Journal; Article
FS 002 Physiology
022 Human Genetics
029 Clinical Biochemistry
LA English
SL English
AB The pineal gland hormone melatonin is well known as a regulator of

circadian rhythmicity, but has also other functions in the central nervous system as well as in the periphery including the maturation of neurons and the regulation of cellular growth and differentiation. Three mechanisms of the hormone's action are currently discussed: a membrane signaling pathway, a nuclear signaling pathway and a receptor-independent radical scavenging function. Melatonin membrane receptors are seven transmembrane receptors and mediate their functions through a G-protein-coupled second messenger pathway. Nuclear melatonin signaling seems to be mediated via the transcription factor RZR/ ***ROR*** , which is an orphan member of the nuclear receptor superfamily. The widespread distribution of the .alpha.-subtype of RZR/ ***ROR*** suggests that this receptor may be an important mediator of those effects of melatonin that can not be explained by membrane receptors or radical scavenging. Interestingly, natural RZR/ ***ROR*** .alpha.' ***knock*** - ***out*** ' mice (staggerer) show severe defects in the development of cerebellar Purkinje cells, a reduced body weight and immunological defects. RZR/ ***ROR*** binds as a monomer to DNA, but also forms homodimers on appropriate binding sites. Natural RZR/ ***ROR*** binding sites have been identified in the regulatory regions of many genes. 5-lipoxygenase, p21(WAF1/CIP1), apolipoprotein A-I, N-myc and Purkinje cell protein 2 may be functionally important target genes. On some of these binding sites RZR/ ***ROR*** competes with other members of the nuclear receptor superfamily (e.g., COUP- TF, RAR and Rev-ErbA) indicating a cross-talk between these transcription factors. RZR/ ***ROR*** often shows in transient transfection assays a high constitutive, i.e. ligand-independent activity. However, under conditions of low constitutive activity a significant and specific stimulation of RZR/ ***ROR*** by low nanomolar concentrations of melatonin and a structurally novel class of thiazolidinediones (lead structure: CGP52608) has been observed. Taken together, the effects of melatonin on transcriptional regulation clearly depend on the expression of RZR/ ***ROR*** and support the concept that the receptor is a mediator of nuclear melatonin signaling.

L3 ANSWER 19 OF 22 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.DUPLICATE
12
AN 1997:366278 BIOSIS
DN PREV199799658211
TI Transcriptional regulation of a Purkinje cell-specific gene through a functional interaction between ROR-alpha and RAR.
AU Matsui, Takashi
CS Dep. Molecular Biol., Univ. Occupational and Environ. Health, 1-1 Iseigaoka, Yahatanishi-ku, Kitakyushu 807 Japan
SO Genes To Cells, (1997) Vol. 2, No. 4, pp. 263-272.
ISSN: 1356-9597.
DT Article
LA English
AB Background: The orphan nuclear receptor ***ROR*** -alpha is highly expressed in the Purkinje cells of the cerebellum during the postnatal development of brain. A recent observation has been made that the ***ROR*** -alpha gene is ***disrupted*** in staggerer mice-which show a cell-autonomous defect in the development of the Purkinje cells. Results: In order to understand the functions of ***ROR*** -alpha in cerebellar development, I attempted to identify its target genes. Transient expression study demonstrated that transcription of the Purkinje cell protein-2 (Pcp-2) gene is activated by ***ROR*** -alpha, which binds as a monomer to a single half-site motif (RORE) within the promoter region. Its transcription was also activated by retinoic acid receptor (RAR) which binds as a heterodimer with RXR to a retinoic acid responsive element (RARE) in the downstream region. Interestingly, the ***ROR*** -alpha-mediated transcription is further activated synergistically by RAR. Conclusion: That the Pcp-2 gene is a target of ***ROR*** -alpha, and is suggested that its transcription is also regulated by RAR.

L3 ANSWER 20 OF 22 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.DUPLICATE
13
AN 1996:123086 BIOSIS
DN PREV199698695221
TI ***Disruption*** of the nuclear hormone receptor ***ROR*** -alpha in staggerer mice.
AU Hamilton, Bruce A. (1); Frankel, Wayne N.; Kerrebrock, Anne W. (1); Hawkins, Trevor L. (1); Fitzhugh, William (1); Kusumi, Kenro (1); Russell, Liane B.; Mueller, Ken L. (1); Van Berkel, Victor (1); Birren, Bruce W. (1); Kruglyak, Leonid (1); Lander, Eric S. (1)
CS (1) Whitehead Inst. Biomed. Research, Nine Cambridge Centre, Cambridge, MA 02142 USA
SO Nature (London), (1996) Vol. 379, No. 6567, pp. 736-739.
ISSN: 0028-0836.
DT Article
LA English
AB Homozygous staggerer (sg) mice show a characteristic severe cerebellar ataxia due to a cell-autonomous defect in the development of Purkinje cells. These cells show immature morphology, synaptic arrangement, biochemical properties and gene expression, and are reduced in numbers. In addition, sg heterozygotes show accelerated dendritic atrophy and cell suggesting that sg has a role in mature Purkinje cells. Effects of this mutation on cerebellar development have been studied for 25 years, but its molecular basis has remained unknown. We have genetically mapped staggerer to an interval of 160 kilobases on mouse chromosome 9 which was found to contain the gene encoding ROR-alpha, a member of the nuclear hormone-receptor superfamily. Staggerer mice were found to carry a deletion within the ROR-alpha gene that prevents translation of the ligand-binding homology domain. We propose a model based on these results, in which ROR-alpha interacts with the thyroid hormone signalling pathway to induce Purkinje-cell maturation.

L3 ANSWER 21 OF 22 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
AN 96163459 EMBASE
DN 1996163459
TI Correction: ***Disruption*** of the nuclear hormone receptor ***ROR*** .alpha. in staggerer mice (Nature Journal (1996) 379 (736-739)).
AU Hamilton B.A.; Frankel W.N.; Kerrebrock A.W.; Hawkins T.L.; FitzHugh W.; Kusumi K.; Russell L.B.; Mueller K.L.; Van Berkel V.; Birren B.W.; Kruglyak L.; Lander E.S.
SO Nature, (1996) 381/6580 (346).
ISSN: 0028-0836 CODEN: NATUAS
CY United Kingdom
DT Journal; Errata
FS 029 Clinical Biochemistry
LA English

L3 ANSWER 22 OF 22 CAPLUS COPYRIGHT 2002 ACS
AN 1996:317547 CAPLUS
DN 125:111831
TI ***Disruption*** of the nuclear hormone receptor ***ROR*** .alpha. in staggerer mice. [Erratum to document cited in CA124:199592]
AU Hamilton, Bruce A.; Frankel, Wayne N.; Kerrebrock, Anne W.; Hawkins, Trevor L.; FitzHugh, William; Kusumi, Kenro; Russell, Liane B.; Mueller, Ken L.; van Berkel, Victor; et al.
CS Whitehead Inst. Biomedical Res., Cambridge, MA, 02142, USA
SO Nature (London) (1996), 381(6580), 346
CODEN: NATUAS; ISSN: 0028-0836
PB Macmillan Magazines
DT Journal
LA English
AB Figure 3a and b is labeled incorrectly. The ROR.alpha.1 cDNA sequence has been submitted to GenBank. The index entries were cor.

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=> s retinoid like orphan receptor gamma or ROR gamma
L4 54 RETINOID LIKE ORPHAN RECEPTOR GAMMA OR ROR GAMMA

=> s l4 and (knockout or knockout or transgen? or disrupt? or deficien?)
L5 14 L4 AND (KNOCKOUT OR KNOCKOUT OR TRANSGEN? OR DISRUPT? OR DEFICIEN?)

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L6 8 DUP REM L5 (6 DUPLICATES REMOVED)

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L6 ANSWER 1 OF 8 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.DUPLICATE 1
AN 2002055739 EMBASE
TI High incidence of T-cell lymphomas in mice ***deficient*** in the retinoid-related orphan receptor ***ROR*** . ***gamma*** ..
AU Ueda E.; Kurebayashi S.; Sakaue M.; Backlund M.; Koller B.; Jetten A.M.
CS A.M. Jetten, Natl. Inst. of Env. Health Sci., 111 T. W. Alexander Drive, Res. Triangle Park., NC 27709-2233, United States. jetten@niehs.nih.gov
SO Cancer Research, (1 Feb 2002) 62/3 (901-909).
Refs: 41
ISSN: 0008-5472 CODEN: CNREA8
CY United States
DT Journal; Article
FS 016 Cancer
025 Hematology
LA English
SL English
AB Nuclear receptors are critical regulators of many physiological processes and have been shown to be involved in a variety of disease processes, including malignant neoplasms. Our laboratory is investigating the function of the retinoid-related orphan receptor .gamma. (***ROR*** . ***gamma*** .) and its possible role in disease. Studies of mice ***deficient*** in the expression of ***ROR*** . ***gamma*** . demonstrated that this receptor plays a crucial role in the regulation of thymopoiesis and lymph node organogenesis. In this study, we show that changes in homeostasis in the thymus of ***ROR*** . ***gamma*** .(-/-) mice are associated with a high incidence of T-cell lymphomas. Over 50% of the ***deficient*** mice of mixed genetic background die within the first 4 months as a result of thymic lymphomas. A high incidence of lymphomas was also observed in ***ROR*** . ***gamma*** .(-/-) 129/SvEv mice. The lymphoblastic cells metastasized frequently to spleen and liver. No other tumor types were detected in any of ***ROR*** . ***gamma*** .(-/-) mice that died during the course of the experiment, and none of the heterozygous mice developed thymic lymphomas. Lymphoma formation was associated with increased cellular proliferation and an increase in the number of apoptotic cells. When placed in culture, the ***ROR*** . ***gamma*** .(-/-) lymphoblastic cells underwent accelerated "spontaneous" apoptosis at a rate similar to that of ***ROR*** . ***gamma*** .(-/-) thymocytes. Upon prolonged culture, several lymphoblastic cell lines could be established. Analysis of the immunophenotype of the lymphoblastic cells showed that the CD4 and CD8 subpopulations varied substantially among different lymphomas. The established cell lines consisted mostly of CD44(-)CD25(+)CD4(-)CD8(-) cells. Our studies indicate that loss of ***ROR*** . ***gamma*** . disturbs homeostasis in the thymus by enhancing apoptosis and cellular proliferation. The latter may enhance the probability of individual cells to acquire genetic alterations that make them escape negative selection and normal differentiation programs and as a consequence lead to increased susceptibility to the development of T-cell lymphoma.

L6 ANSWER 2 OF 8 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.DUPLICATE 2
AN 2002:372769 BIOSIS
DN PREV200200372769
TI Regulation of the TCRalpha repertoire by the survival window of CD4+CD8+ thymocytes.
AU Guo, Jian; Hawwari, Abbas; Li, Hong; Sun, Zuoming; Mahanta, Sanjeev K.; Littman, Dan R.; Krangel, Michael S.; He, You-Wen (1)
CS (1) Department of Immunology, Duke University Medical Center, Durham, NC, 27710: he000004@mc.duke.edu USA
SO Nature Immunology, (May, 2002) Vol. 3, No. 5, pp. 469-476. print.
ISSN: 1529-2908.
DT Article
LA English
AB T cell receptor (TCR) alpha alleles undergo primary and secondary rearrangement in double-positive (DP) thymocytes. By analyzing TCRalpha rearrangement in orphan nuclear receptor RORgamma- ***deficient*** mice, in which the DP lifespan is shorter, and in Bcl-xL- ***transgenic*** mice, in which the DP lifespan is extended, we show that the progression of secondary Valpha to Jalpha rearrangements is controlled by DP thymocyte survival. In addition, because Bcl-xL induces a bias towards 3' Jalpha usage in peripheral T cells, we conclude that the programmed cell death of DP thymocytes is not simply a consequence of failed positive selection. Rather, it limits the progression of rearrangement along the Jalpha locus and the opportunities for positive selection, thereby regulating the TCRalpha repertoire.

L6 ANSWER 3 OF 8 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
AN 2001:480965 BIOSIS
DN PREV200100480965
TI Accelerated apoptosis in thymocytes and induction of T cell lymphoma formation in RORgamma- ***deficient*** mice.
AU Kurebayashi, Shogo (1); Ueda, Eiichiro (1); Jetten, Anton M. (1)
CS (1) NIEHS/NIH, RTP, NC USA
SO Proceedings of the American Association for Cancer Research Annual Meeting, (March, 2001) Vol. 42, pp. 552. print.
Meeting Info.: 92nd Annual Meeting of the American Association for Cancer Research New Orleans, LA, USA March 24-28, 2001
ISSN: 0197-016X.
DT Conference
LA English
SL English

L6 ANSWER 4 OF 8 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
AN 2001:483941 BIOSIS
DN PREV200100483941
TI In vivo function of a differentiation inhibitor, Id2.
AU Yokota, Yoshifumi (1); Mori, Seiichi; Narumi, Osamu; Kitajima, Kazuhito
CS (1) Department of Biochemistry, Fukui Medical University, Shimoaizuki 23-3, Matsuoka, Fukui, 910-1193: yyokota@fmsrsa.fukui-med.ac.jp Japan
SO IUBMB Life, (April, 2001) Vol. 51, No. 4, pp. 207-214. print.
ISSN: 1521-6543.
DT General Review
LA English
SL English
AB Cell differentiation is an essential process for the development of various cell types that constitute multicellular organisms. During development, the large family of factors bearing a helix-loop-helix (HLH) motif participates profoundly in this process and these factors serve as good experimental tools for investigating mechanisms underlying tissue-specific differentiation. The HLH family includes both positive and negative regulators of cell differentiation: basic HLH (bHLH)-type transcription factors and Id proteins, respectively. Following an exciting decade focusing on bHLH factors, advances achieved in studies of the inhibitory factors in the last couple of years have placed them in the front line of the research on differentiation and proliferation control. Here, we present and discuss recent results obtained using Id2- ***deficient*** mice, which manifest intriguing phenotypes in various systems.

L6 ANSWER 5 OF 8 CAPLUS COPYRIGHT 2002 ACS
AN 2001:715683 CAPLUS
DN 136:31758
TI The ROR nuclear orphan receptor subfamily: Critical regulators of multiple biological processes
AU Jetten, Anton M.; Kurebayashi, Shogo; Ueda, Eiichiro
CS Cell Biology Section Division of Intramural Research National Institute of Environmental Health Sciences, National Institutes of Health, Research Triangle Park, NC, 27709, USA
SO Progress in Nucleic Acid Research and Molecular Biology (2001), 69, 205-247
CODEN: PNMBAF; ISSN: 0079-6603
PB Academic Press
DT Journal; General Review
LA English
AB A review. The nuclear receptor superfamily, a group of structurally related, ligand-dependent transcription factors, includes a large no. of orphan receptors for which no ligand has yet been identified. These proteins function as key regulators of many physiol. processes that occur during embryonic development and in the adult. The retinoid-related orphan receptors (RORs) .alpha., .beta., and .gamma. comprise one nuclear orphan receptor gene subfamily. RORs exhibit a modular structure that is characteristic for nuclear receptors; the DNA-binding domain is highly conserved and the ligand-binding domain is moderately conserved among RORs. By a combination of alternative promoter usage and exon splicing, each ROR gene generates several isoforms that differ only in their N-terminus. RORs bind as monomers to specific ROR response elements (ROREs) consisting of the consensus core motif AGGTCA preceded by a 5-bp A/T-rich sequence. RORE-dependent transcriptional activation by RORs is cell type-specific and mediated through interactions with nuclear cofactors. RORs have been shown to interact with certain corepressors as well as coactivators, suggesting that RORs are not constitutively active but that their activity is under some regulatory control. RORs likely can assume at least two different conformations: a repressive state, which allows interaction with corepressor complexes, and an active state, which promotes binding of coactivator complexes. Whether the transition between these two states is regulated by ligand binding and/or by phosphorylation remains to be detd. Ca2+/calmodulin-dependent kinase IV (CaMKIV) can dramatically enhance ROR-mediated transcriptional activation. This stimulation involves CaMKIV-mediated phosphorylation not of RORs, but likely of specific nuclear cofactors that interact with RORs. ROR.alpha. is widely expressed. In the cerebellum, its expression is limited to the Purkinje cells. ROR.alpha.-/- mice and the natural ROR.alpha.- ***deficient*** staggerer mice exhibit severe cerebellar ataxia due to a defect in Purkinje cell development. In addn., these mice have thin long bones, suggesting a role for ROR.alpha. in bone metab., and develop severe atherosclerosis when placed on a high-fat diet. Expression of ROR.beta. is very restricted. ROR.beta. is highly expressed in different parts of the neurophotoendocrine system, the pineal gland, the retina, and suprachiasmatic nuclei, suggesting a role in the control of circadian rhythm. This is supported by observations showing alterations in circadian behavior in ROR.beta.-/- mice. ***ROR*** . ***gamma*** ., which is most highly expressed in the thymus, plays an important role in thymopoiesis. Thymocytes from ***ROR*** . ***gamma*** .-/- mice undergo accelerated apoptosis. The induction of apoptosis is, at least in part, due to a down-regulation of the expression of the antiapoptotic gene Bcl-XL. In addn. to the thymic phenotype, ***ROR***. ***gamma*** .-/- mice lack lymph nodes, indicating that ***ROR*** . ***gamma*** . is essential for lymph node organogenesis. Overexpression of ***ROR*** . ***gamma*** . has been shown to inhibit T cell receptor-mediated apoptosis in T cell hybridomas and to repress the induction of Fas-ligand and interleukin 2. These studies demonstrate that RORs play crit. roles in the regulation of a variety of physiol. processes. Further

characterization of the mechanisms of action of RORs will not only lead to the identification of ROR target genes and provide addnl. insight into their normal physiol. functions, but will also det. their roles in disease. (c) 2001 Academic Press.
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ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 6 OF 8 CAPLUS COPYRIGHT 2002 ACS
AN 2000:291059 CAPLUS
DN 132:320946
TI Human ***retinoid*** - ***like*** ***orphan*** ***receptor*** ***gamma***
IN Wu, Lin; Chen, Jin-long
PA Tularik Inc., USA
SO PCT Int. Appl., 69 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2000024757	A1	20000504	WO 1999-US24309	19991018

W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRAI US 1998-178358 19981023
AB The invention provides isolated nucleic acid and amino acid sequences of hROR.gamma., antibodies to hROR.gamma., ***transgenic*** animals, methods of identifying ligands for hROR.gamma., and methods of screening for modulators of hROR.gamma.. Members of ***ROR*** . ***gamma*** . are preferentially expressed in thymus, T cell lymphomas and skeletal muscle; contain DNA-binding moiety; bind to ligands such as melatonin; and are involved in regulation of immune system (e.g. transcriptional regulation in allergies and inflammatory reactions) and adipocyte differentiation.
RE.CNT 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 7 OF 8 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.DUPLICATE 3
AN 2000:440535 BIOSIS
DN PREV200000440535
TI Retinoid-related orphan receptor gamma (RORgamma) is essential for lymphoid organogenesis and controls apoptosis during thymopoiesis.
AU Kurebayashi, Shogo; Ueda, Eiichiro; Sakaue, Morito; Patel, Dhavalkumar D.; Medvedev, Alex; Zhang, Feng; Jetten, Anton M. (1)
CS (1) Cell Biology Section, Laboratory of Pulmonary Pathology, National Institute of Environmental Health Sciences, National Institutes of Health, Research Triangle Park, NC, 27709 USA
SO Proceedings of the National Academy of Sciences of the United States of America, (August 29, 2000) Vol. 97, No. 18, pp. 10132-10137. print.
ISSN: 0027-8424.
DT Article
LA English
SL English
AB To identify the physiological functions of the retinoid-related orphan receptor gamma (RORgamma), a member of the nuclear receptor superfamily, mice ***deficient*** in RORgamma function were generated by targeted ***disruption*** . RORgamma-/-mice lack peripheral and mesenteric lymph nodes and Peyer's patches, indicating that RORgamma expression is indispensable for lymph node organogenesis. Although the spleen is enlarged, its architecture is normal. The number of peripheral blood CD3+ and CD4+ lymphocytes is reduced 6- and 10-fold, respectively, whereas the number of circulating B cells is normal. The thymus of RORgamma-/- mice contains 74.4% +- 8.9% fewer thymocytes than that of wild-type mice. Flow cytometric analysis showed a decrease in the CD4+CD8+ subpopulation. Terminal deoxynucleotidyltransferase-mediated dUTP nick end labeling (TUNEL) staining demonstrated a 4-fold increase in apoptotic cells in the cortex of the thymus of RORgamma-/- mice. The latter was supported by the observed increase in annexin V-positive cells. RORgamma-/- thymocytes placed in culture exhibit a dramatic increase in the rate of "spontaneous" apoptosis. This increase is largely associated with CD4+CD8+ thymocytes and may, at least in part, be related to the greatly reduced level of expression of the anti-apoptotic gene Bcl-XL. Flow cytometric analysis demonstrated a 6-fold rise in the percentage of cells in the S phase of the cell cycle among thymocytes from RORgamma-/- mice. Our observations indicate that RORgamma is essential for lymphoid organogenesis and plays an important regulatory role in thymopoiesis. Our findings support a model in which RORgamma negatively controls apoptosis in thymocytes.

L6 ANSWER 8 OF 8 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.DUPLICATE 4
AN 2000211217 EMBASE
TI Down-regulation of the orphan nuclear receptor ***ROR*** . ***gamma*** .t is essential for T lymphocyte maturation.
AU He Y.-W.; Beers C.; Deftos M.L.; Ojala E.W.; Forbush K.A.; Bevan M.J.
CS Dr. M.J. Bevan, Howard Hughes Medical Institute, Department of Immunology, Univ. of Washington Sch. of Medicine, Seattle, WA 98195, United States. mbevan@u.washington.edu
SO Journal of Immunology, (2000) 164/11 (5668-5674).
Refs: 32
ISSN: 0022-1767 CODEN: JOIMA3
CY United States
DT Journal; Article
FS 026 Immunology, Serology and Transplantation
LA English
SL English
AB Thymocyte development is a tightly regulated process. CD4+ CD8+ double-positive (DP) immature thymocytes exhibit distinct phenotypic features from mature T cells; they express only 10% of surface TCR that are found on mature T cells and do not proliferate and produce IL-2 in response to stimulation. In this report we show that ***transgenic*** expression of the orphan nuclear receptor ***ROR*** . ***gamma*** .t in mature T cells down-regulates their surface TCR expression. The ***ROR*** . ***gamma*** .t ***transgene*** inhibits IL-2 production by mature T cells, and this inhibition may be partially due to the inhibitory effect of ***ROR*** . ***gamma*** .t on c-Rel transcription. Furthermore, ectopic expression of ***ROR*** . ***gamma*** .t inhibits the proliferation of mature and immature T cells. These results, together with its predominant expression in DP thymocytes, suggest that ***ROR*** . ***gamma*** .t controls these distinct phenotypic features of DP thymocytes. Our data suggest that down-regulation of ***ROR*** . ***gamma*** .t expression in thymocytes is essential for their maturation.

=> d his

(FILE 'HOME' ENTERED AT 10:46:32 ON 29 AUG 2002)

FILE 'BIOSIS, EMBASE, CAPLUS' ENTERED AT 10:47:00 ON 29 AUG 2002
L1 923 S RETINOID LIKE ORPHAN RECEPTOR OR ROR
L2 38 S L1 (3S) (KNOCKOUT OR KNOCK OUT OR TRANSGEN? OR DISRUPT?)
L3 22 DUP REM L2 (16 DUPLICATES REMOVED)

FILE 'STNGUIDE' ENTERED AT 10:59:51 ON 29 AUG 2002

FILE 'BIOSIS, EMBASE, CAPLUS' ENTERED AT 11:12:03 ON 29 AUG 2002
L4 54 S RETINOID LIKE ORPHAN RECEPTOR GAMMA OR ROR GAMMA
L5 14 S L4 AND (KNOCKOUT OR KNOCKOUT OR TRANSGEN? OR DISRUPT? OR DEF
L6 8 DUP REM L5 (6 DUPLICATES REMOVED)

=> s l4 (3a) (murine or mouse or mice)
L7 15 L4 (3A) (MURINE OR MOUSE OR MICE)

=> dup rem l7
PROCESSING COMPLETED FOR L7
L8 9 DUP REM L7 (6 DUPLICATES REMOVED)

=> d bib abs

L8 ANSWER 1 OF 9 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.DUPLICATE 1
AN 2002055739 EMBASE
TI High incidence of T-cell lymphomas in mice deficient in the retinoid-related orphan receptor ROR.gamma..
AU Ueda E.; Kurebayashi S.; Sakaue M.; Backlund M.; Koller B.; Jetten A.M.
CS A.M. Jetten, Natl. Inst. of Env. Health Sci., 111 T. W. Alexander Drive, Res. Triangle Park., NC 27709-2233, United States. jetten@niehs.nih.gov
SO Cancer Research, (1 Feb 2002) 62/3 (901-909).
Refs: 41
ISSN: 0008-5472 CODEN: CNREA8
CY United States
DT Journal; Article
FS 016 Cancer
025 Hematology
LA English
SL English
AB Nuclear receptors are critical regulators of many physiological processes and have been shown to be involved in a variety of disease processes, including malignant neoplasms. Our laboratory is investigating the function of the retinoid-related orphan receptor .gamma. (ROR.gamma.) and its possible role in disease. Studies of mice deficient in the expression of ROR.gamma. demonstrated that this receptor plays a crucial role in the regulation of thymopoiesis and lymph node organogenesis. In this study, we show that changes in homeostasis in the thymus of ***ROR*** . ***gamma*** .(-/-) ***mice*** are associated with a high incidence of T-cell lymphomas. Over 50% of the deficient mice of mixed genetic background die within the first 4 months as a result of thymic lymphomas. A high incidence of lymphomas was also observed in .***ROR*** . ***gamma*** .(-/-) 129/SvEv ***mice*** . The lymphoblastic cells metastasized frequently to spleen and liver. No other tumor types were detected in any of ***ROR*** . ***gamma*** .(-/-) ***mice*** that died during the course of the experiment, and none of the heterozygous mice developed thymic lymphomas. Lymphoma formation was associated with increased cellular proliferation and an increase in the number of

apoptotic cells. When placed in culture, the ROR.gamma.(-/-) lymphoblastic cells underwent accelerated "spontaneous" apoptosis at a rate similar to that of ROR.gamma.(-/-) thymocytes. Upon prolonged culture, several lymphoblastic cell lines could be established. Analysis of the immunophenotype of the lymphoblastic cells showed that the CD4 and CD8 subpopulations varied substantially among different lymphomas. The established cell lines consisted mostly of CD44(-)CD25(+)CD4(-)CD8(-) cells. Our studies indicate that loss of ROR.gamma. disturbs homeostasis in the thymus by enhancing apoptosis and cellular proliferation. The latter may enhance the probability of individual cells to acquire genetic alterations that make them escape negative selection and normal differentiation programs and as a consequence lead to increased susceptibility to the development of T-cell lymphoma.

=> d bib abs 2-
YOU HAVE REQUESTED DATA FROM 8 ANSWERS - CONTINUE? Y/(N):y

L8 ANSWER 2 OF 9 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
AN 2002:395669 BIOSIS
DN PREV200200395669
TI RORgamma overexpression and c-myc down-modulation in retrovirally-induced T-cell lymphomas.
AU Dudley, Jaquelin P. (1); Mertz, Jennifer A. (1); Lozano, Mary (1); Broussard, Dana R. (1)
CS (1) University of Texas at Austin, Austin, TX USA
SO Proceedings of the American Association for Cancer Research Annual Meeting, (March, 2002) Vol. 43, pp. 655. print.
Meeting Info.: 93rd Annual Meeting of the American Association for Cancer Research San Francisco, California, USA April 06-10, 2002
ISSN: 0197-016X.
DT Conference
LA English

L8 ANSWER 3 OF 9 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.DUPLICATE 2
AN 2002177042 EMBASE
TI Regulation of the TCR.alpha. repertoire by the survival window of CD4(+)CD8(+) thymocytes.
AU Guo J.; Hawwari A.; Li H.; Sun Z.; Mahanta S.K.; Littman D.R.; Krangel M.S.; He Y.-W.
CS Y.-W. He, Department of Immunology, Duke University Medical Center, Durham, NC 27710, United States. he000004@mc.duke.edu
SO Nature Immunology, (2002) 3/5 (469-476).
Refs: 46
ISSN: 1529-2908 CODEN: NIAMCZ
CY United States
DT Journal; Article
FS 025 Hematology
026 Immunology, Serology and Transplantation
LA English
SL English
AB T cell receptor (TCR) .alpha. alleles undergo primary and secondary rearrangement in double-positive (DP) thymocytes. By analyzing TCR.alpha. rearrangement in orphan nuclear receptor ***ROR*** . ***gamma*** .-deficient ***mice*** , in which the DP lifespan is shorter, and in Bcl-x(L)-transgenic mice, in which the DP lifespan is extended, we show that the progression of secondary V(.alpha.) to J(.alpha.) rearrangements is controlled by DP thymocyte survival. In addition, because Bcl-x(L) induces a bias towards 3' J(.alpha.) usage in peripheral T cells, we conclude that the programmed cell death of DP thymocytes is not simply a consequence of failed positive selection. Rather, it limits the progression of rearrangement along the J(.alpha.) locus and the opportunities for positive selection, thereby regulating the TCR.alpha. repertoire.

L8 ANSWER 4 OF 9 CAPLUS COPYRIGHT 2002 ACS
AN 2001:715683 CAPLUS
DN 136:31758
TI The ROR nuclear orphan receptor subfamily: Critical regulators of multiple biological processes
AU Jetten, Anton M.; Kurebayashi, Shogo; Ueda, Eiichiro
CS Cell Biology Section Division of Intramural Research National Institute of Environmental Health Sciences, National Institutes of Health, Research Triangle Park, NC, 27709, USA
SO Progress in Nucleic Acid Research and Molecular Biology (2001), 69, 205-247
CODEN: PNMBAF; ISSN: 0079-6603
PB Academic Press
DT Journal; General Review
LA English
AB A review. The nuclear receptor superfamily, a group of structurally related, ligand-dependent transcription factors, includes a large no. of orphan receptors for which no ligand has yet been identified. These proteins function as key regulators of many physiol. processes that occur during embryonic development and in the adult. The retinoid-related orphan receptors (RORs) .alpha., .beta., and .gamma. comprise one nuclear orphan receptor gene subfamily. RORs exhibit a modular structure that is characteristic for nuclear receptors; the DNA-binding domain is highly conserved and the ligand-binding domain is moderately conserved among RORs. By a combination of alternative promoter usage and exon splicing, each ROR gene generates several isoforms that differ only in their N-terminus. RORs bind as monomers to specific ROR response elements (ROREs) consisting of the consensus core motif AGGTCA preceded by a 5-bp A/T-rich sequence. RORE-dependent transcriptional activation by RORs is cell type-specific and mediated through interactions with nuclear cofactors. RORs have been shown to interact with certain corepressors as well as coactivators, suggesting that RORs are not constitutively active but that their activity is under some regulatory control. RORs likely can assume at least two different conformations: a repressive state, which allows interaction with corepressor complexes, and an active state, which promotes binding of coactivator complexes. Whether the transition between these two states is regulated by ligand binding and/or by phosphorylation remains to be detd. Ca2+/calmodulin-dependent kinase IV (CaMKIV) can dramatically enhance ROR-mediated transcriptional activation. This stimulation involves CaMKIV-mediated phosphorylation not of RORs, but likely of specific nuclear cofactors that interact with RORs. ROR.alpha. is widely expressed. In the cerebellum, its expression is limited to the Purkinje cells. ROR.alpha.-/- mice and the natural ROR.alpha.-deficient staggerer mice exhibit severe cerebellar ataxia due to a defect in Purkinje cell development. In addn., these mice have thin long bones, suggesting a role for ROR.alpha. in bone metab., and develop severe atherosclerosis when placed on a high-fat diet. Expression of ROR.beta. is very restricted. ROR.beta. is highly expressed in different parts of the neurophotoendocrine system, the pineal gland, the retina, and suprachiasmatic nuclei, suggesting a role in the control of circadian rhythm. This is supported by observations showing alterations in circadian behavior in ROR.beta.-/- mice. ROR.gamma., which is most highly expressed in the thymus, plays an important role in thymopoiesis. Thymocytes from ***ROR*** . ***gamma*** .-/- ***mice*** undergo accelerated apoptosis. The induction of apoptosis is, at least in part, due to a down-regulation of the expression of the antiapoptotic gene Bcl-XL. In addn. to the thymic phenotype, ***ROR*** . ***gamma*** .-/- ***mice*** lack lymph nodes, indicating that ROR.gamma. is essential for lymph node organogenesis. Overexpression of ROR.gamma. has been shown to inhibit T cell receptor-mediated apoptosis in T cell hybridomas and to repress the induction of Fas-ligand and interleukin 2. These studies demonstrate that RORs play crit. roles in the regulation of a variety of physiol. processes. Further characterization of the mechanisms of action of RORs will not only lead to the identification of ROR target genes and provide addnl. insight into their normal physiol. functions, but will also det. their roles in disease. (c) 2001 Academic Press.
RE.CNT 170 THERE ARE 170 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 5 OF 9 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.DUPLICATE 3
AN 2000317789 EMBASE
TI Retinoid-related orphan receptor .gamma.(ROR.gamma.)is essential for lymphoid organogenesis and controls apoptosis during thymopoiesis.
AU Kurebayashi S.; Ueda E.; Sakaue M.; Patel D.D.; Medvedev A.; Zhang F.; Jetten A.M.
CS A.M. Jetten, Laboratory of Pulmonary Pathology, Natl. Inst. of Envtl. Health Sci., National Institute of Health, Research Triangle Park, NC 27709, United States. jetten@niehs.nih.gov
SO Proceedings of the National Academy of Sciences of the United States of America, (29 Aug 2000) 97/18 (10132-10137).
ISSN: 0027-8424 CODEN: PNASA6
CY United States
DT Journal; Article
FS 029 Clinical Biochemistry
LA English
SL English
AB To identify the physiological functions of the retinoid-related orphan receptor .gamma. (ROR.gamma.), a member of the nuclear receptor superfamily, ***mice*** deficient in ***ROR*** . ***gamma*** . function were generated by targeted disruption. ***ROR*** . ***gamma*** .(-/-) ***mice*** lack peripheral and mesenteric lymph nodes and Peyer's patches, indicating that ROR.gamma. expression is indispensable for lymph node organogenesis. Although the spleen is enlarged, its architecture is normal. The number of peripheral blood CD3+ and CD4+ lymphocytes is reduced 6- and 10-fold, respectively, whereas the number of circulating B cells is normal. The thymus of ***ROR*** . ***gamma*** .(-/-) ***mice*** contains 74.4% .+-. 8.9% fewer thymocytes than that of wild-type mice. Flow cytometric analysis showed a decrease in the CD4+CD8+ subpopulation. Terminal deoxynucleotidyltransferase-mediated dUTP nick end labeling (TUNEL) staining demonstrated a 4-fold increase in apoptotic cells in the cortex of the thymus of ***ROR*** . ***gamma*** .(-/-) ***mice*** . The latter was supported by the observed increase in annexin V-positive cells. ROR.gamma.(-/-) thymocytes placed in culture exhibit a dramatic increase in the rate of 'spontaneous' apoptosis. This increase is largely associated with CD4+CD8+ thymocytes and may, at least in part, be related to the greatly reduced level of expression of the anti-apoptotic gene Bcl-X(L). Flow cytometric analysis demonstrated a 6-fold rise in the percentage of cells in the S phase of the cell cycle among thymocytes from ***ROR*** . ***gamma*** .(-/-) ***mice*** . Our observations indicate that ROR.gamma., is essential for lymphoid organogenesis and plays an important regulatory role in thymopoiesis. Our findings support a model in which ROR.gamma. negatively controls apoptosis in thymocytes.

L8 ANSWER 6 OF 9 CAPLUS COPYRIGHT 2002 ACS
AN 1999:803226 CAPLUS

DN 132:106901
TI ROR.gamma.T, a thymus-specific isoform of the orphan nuclear receptor ROR.gamma./TOR, is up-regulated by signaling through the pre-T cell receptor and binds to the TEA promoter
AU Villey, Isabelle; De Chasseval, Regina; De Villartay, Jean-Pierre
CS INSERM U429, Hopital Necker Enfants Malades, Paris, F-75015, Fr.
SO European Journal of Immunology (1999), 29(12), 4072-4080
CODEN: EJIMAF; ISSN: 0014-2980
PB Wiley-VCH Verlag GmbH
DT Journal
LA English
AB TEA (T early .alpha.) is a genetic element located upstream of the TCR-J.alpha. cluster. Thymocytes from mice carrying a targeted deletion of TEA do not rearrange their TCR.alpha. locus on a window spanning the 1st 9 J.alpha. segments. This led the authors to the hypothesis of TEA having a "rearrangement focusing" activity on the 5' side of the TCR-J.alpha. region. The authors analyzed DNAseI and "phylogenetic" footprints within the TEA promoter to identify transacting factors that could account for its regulatory function on DNA accessibility. One of these footprints corresponded to a putative DNA-binding site for an orphan nuclear receptor of the ROR/RZR family. The ROR.gamma.T cDNA clone was isolated from a thymus library using a probe corresponding to the DNA-binding domain of ROR.gamma./TOR. ROR.gamma.T is a thymus-specific isoform of ROR.gamma., expressed almost exclusively in immature double-pos. thymocytes. ROR.gamma.T binds, to the TEA promoter in vitro. Lastly, the expression of ROR.gamma.T is stimulated in 2 situations that mimic activation through the pre-TCR and in which the thymocytes have their TCR-.alpha. locus in an "open", yet unrearranged DNA configuration. The authors propose that the expression of ROR.gamma.T may be part of the pre-TCR activation cascade leading to the maturation of .alpha./.beta. T cells and may participate in the regulation of DNA accessibility in the TCR-J.alpha. locus.
RE.CNT 50 THERE ARE 50 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 7 OF 9 CAPLUS COPYRIGHT 2002 ACS
AN 1999:66470 CAPLUS
DN 130:266309
TI ROR.gamma.t, a novel isoform of an orphan receptor, negatively regulates Fas ligand expression and IL-2 production in T cells
AU He, You-Wen; Deftos, Michael L.; Ojala, Ethan W.; Bevan, Michael J.
CS Department of Immunology and Howard Hughes Medical Institute, University of Washington, Seattle, WA, 98195, USA
SO Immunity (1998), 9(6), 797-806
CODEN: IUNIEH; ISSN: 1074-7613
PB Cell Press
DT Journal
LA English
AB The authors have identified ROR.gamma.t, a novel, thymus-specific isoform of the orphan nuclear receptor ROR.gamma. that is expressed predominantly in CD4+ CD8+ double-pos. thymocytes. Ectopic expression of ROR.gamma.t protects T cell hybridomas from activation-induced cell death by inhibiting the upregulation of Fas ligand. Following hybridoma stimulation, ROR.gamma.t also inhibits IL-2 prodn. but does not affect the induction of Nur-77 and Egr-3 nor the upregulation of CD69. Both the ligand-binding and DNA-binding domains of ROR.gamma.t are required for this effect. The authors propose that the role of ROR.gamma.t expression in immature thymocytes is to inhibit Fas ligand expression and cytokine secretion following engagement of their TCR during pos. or neg. selection.
RE.CNT 61 THERE ARE 61 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 8 OF 9 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.DUPLICATE 4
AN 97383755 EMBASE
DN 1997383755
TI Genomic structure and chromosomal mapping of the nuclear orphan receptor ROR.gamma. (RORC) gene.
AU Medvedev A.; Chistokhina A.; Hirose T.; Jetten A.M.
CS A.M. Jetten, Cell Biology Section, Laboratory of Pulmonary Pathobiology, Natl. Inst. of Envtl. Hlth. Sciences, Research Triangle Park, NC 27709, United States. jetten@niehs.nih.gov
SO Genomics, (1997) 46/1 (93-102).
Refs: 43
ISSN: 0888-7543 CODEN: GNMCEP
CY United States
DT Journal; Article
FS 022 Human Genetics
LA English
SL English
AB The nuclear orphan receptor subfamily ROR/RZR is part of the steroid and thyroid hormone/retinoid receptor superfamily and consists of three different genes, .alpha., .beta., .gamma.. In this study, we determined the genomic structure of ***mouse*** ***ROR*** . ***gamma*** and the chromosomal localization of both ***mouse*** ***ROR*** . ***gamma*** . and human ROR.gamma. (HGMW-approved symbol RORC). The genomic structure of the ***mouse*** ***ROR*** . ***gamma*** . gene was derived from the analysis of P1 vector clones containing large genomic fragments encoding ROR.gamma.. These results revealed that the mROR.gamma. gene has a complex structure consisting of 11 exons separated by 10 introns spanning more than 21 kb of genomic DNA. The DNA-binding domain is contained in two exons, 3 and 4, each encoding one zinc-finger. The splice site between exon 3 and exon 4 is identical to that found in RAR and TR3 receptors. ROR.gamma. is expressed as two mRNAs, 2.3 and 3.0 kb in size, that are derived by the use of alternative polyadenylation signals. We show by fluorescence in situ hybridization that the ***mouse*** ***ROR*** . ***gamma*** . gene is located on chromosome 3, in a region that corresponds to band 3F2.1-2.2. The human ROR.gamma. was mapped to chromosome region 1q21. The results demonstrate that the ROR.gamma. genes are located in chromosomal regions that are syntenic between mouse and human.

L8 ANSWER 9 OF 9 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.DUPLICATE 5
AN 1997:42662 BIOSIS
DN PREV199799334650
TI Cloning of a cDNA encoding the ***murine*** orphan receptor RZR/ ***ROR*** - ***gamma*** and characterization of its response element.
AU Medvedev, Alexander; Yan, Zhong-Hua; Hirose, Takahisa; Giguere, Vincent; Jetten, Anton M. (1)
CS (1) Cell Biol. Sect., Lab. Pulmonary Pathobiol., Natl. Inst. Environ. Health Sci., Natl. Inst. Health, Research Triangle Park, NC 27709 USA
SO Gene (Amsterdam), (1996) Vol. 181, No. 1-2, pp. 199-206.
ISSN: 0378-1119.
DT Article
LA English
AB In this study, we describe the cloning of the mouse homologue of the orphan receptor, RZR/ROR-gamma, a member of the nuclear receptor superfamily, from a mouse muscle cDNA library. The amino acid sequence of ***mouse*** ***ROR*** - ***gamma*** (mROR-gamma) is highly homologous to that of human ROR-gamma, with an overall identity of 88%. Northern blot analysis using RNA from different tissues showed that mROR-gamma was found to be highly expressed in skeletal muscle, liver and kidney. Analysis of the ROR-gamma-response element using in vitro synthesized ROR-gamma revealed that it binds as a monomer to response elements composed of a single core motif GGTCA preceded by a 6 bp AT-rich sequence. The ROR-gamma-binding specificity was further defined by mutational analysis of the consensus RORE. ROR-gamma was able to activate RORE-dependent transcription of the CAT reporter gene in mouse fibroblast D1 cells. RORo-alpha-1 and ROR-gamma inhibit the transactivation induced by GAL4(DBD)-ROR-gamma in fibroblast D1 cells suggesting that these receptors compete for binding to the same coactivators.

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